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Broms, Ulla Heidi

2012

Broms , U H , Pennanen , M , Patja , K , Ollila , H , Korhonen , T , Kankaanpää , A , Haukkala , A , Tuulio-Henriksson , A , Koskenvuo , M , Kronholm , E , Laatikainen , T , Peltonen , M , Partonen , T & Kaprio , J 2012 , ' Diurnal evening type is associated with current smoking, nicotine dependence and nicotine intake in the population based national FINRISK 2007 study ' , Addiction Research & Therapy , vol. 2012 , pp. S2 . https://doi.org/10.4172/2155-6105.S2-00

http://hdl.handle.net/10138/233995
https://doi.org/10.4172/2155-6105.S2-002

publishedVersion

Published in final edited form as:
J Addict Res Ther. 2012 January 25; Suppl 2: .

Diurnal Evening Type is Associated with Current Smoking, Nicotine Dependence and Nicotine Intake in the Population Based National FINRISK 2007 Study

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Abstract

Aims—To examine whether smoking habits, nicotine dependence (ND) and plasma cotinine levels differ by diurnal type.

Design—Data originated from the national FINRISK 2007 survey. Regression analyses were calculated to examine the association between diurnal type and smoking status, ND, and nicotine intake.

Participants—7091 FINRISK participants with smoking and diurnal type information and a subset of 1746 ever smokers with detailed smoking, and ND assessments.

Measurements—Diurnal type assessed with a six-item sum scale was categorized as morning, intermediate and evening type. Smoking status was determined as current (daily or occasional), former, and never smokers. ND was measured with the Fagerström Test for Nicotine Dependence (FTND), the Hooked on Nicotine Checklist (HONC), and the Nicotine Dependence Syndrome Scale (NDSS). For current smokers, plasma cotinine was analyzed as biochemical measurement of nicotine intake.

Findings—Evening type was associated with current smoking (OR=1.66, 95% CI 1.40, 1.97). A significant association with diurnal type was seen for FTND among men (beta= -0.46, 95% CI -0.72, -0.21), sexes combined for HONC (beta= -0.31, 95% CI -0.52, -0.11) and NDSS (beta= -0.86, 95% CI -1.43, -0.29) and for cotinine among men (beta= -0.73, 95% CI -1.16, -0.29). Adjustment for depressive symptoms attenuated the association of diurnal type with NDSS to be non-significant.

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Conflict of Interest Statement

Dr. Kaprio has served as a consultant to Pfizer on pharmacogenetics of smoking cessation and nicotine dependence. Dr. Broms has served as a consultant to Pfizer on nicotine dependence measurements. Dr. Korhonen has served as a consultant on nicotine dependence to Pfizer.

Conclusions—Diurnal type was associated with multiple ND measures and nicotine intake, interestingly more so among men. Evening type persons are at higher risk of dependence, but depressive symptoms attenuates this association clearly.

Keywords

Adults; Smoking; Nicotine dependence; Diurnal type; Chronotype; Eveningness; Fagerström test for nicotine dependence; Nicotine dependence syndrome scale; Hooked on nicotine checklist; Cotinine

Introduction

People have different sleeping rhythms, diurnal types, which have been shown to be associated with different health and behavioral risk factors. Diurnal type or chronotype refers to relatively stable trait-like interindividual differences in temporal organization of individuals sleep/wake behavior and other physiological functions [1]. The notion can be seen as a continuum between two extreme types: morning and evening type. In nationwide Finnish Twin Cohort of adult twins [2] most adults were intermediate types, with about 27% being morning types and 10% evening types.

Earlier studies, mostly with relatively small sample sizes, have demonstrated an association between diurnal type and smoking, such as among university students in Japan [3], 14 to 94 year olds in Germany and Austria [4], Hungarian adolescents [5], as well as Finnish adolescents [6] and adults [7]. These are in line with our recent study of Finnish twins [7] indicating that by using a single question on diurnal type, the Fagerström Test for Nicotine Dependence (FTND) [8] and DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) diagnosis of nicotine dependence (ND) [9] the evening type was strongly associated with not only being a smoker but also with ND. These associations persisted even after potential confounders associated with diurnal type and smoking such as mood and alcohol use [10-13] were taken into account.

The association of smoking and evening type could be explained by genetic and environmental factors involved in the dopamine and/or opioid systems. These are the key elements in feelings of pleasure and also in development of addiction. Moreover, it is known that people with attention deficit hyperactivity disorder are mainly evening types and more prone to develop addictions than others [14]. Gender differences in the association between diurnal type and smoking have been found so that risk of current smoking among evening types was higher among women compared to men [7]. One potential reason might be the faster nicotine metabolism of women compared to men [15].

Nicotine is a psychoactive stimulant, and there may be some association between this stimulant effect and the phase of circadian rhythms. Nicotine is a direct agonist of nicotinic acetylcholine receptors (nAChR) and activates mesolimbic dopaminergic pathways [16,17]. Melatonin levels are associated with chronotype. Dim light melatonin onset, but not sleep onset nor melatonin offset times, has been shown to be related to chronotype [18]. In addition, it is shown that melatonin serum concentrations are lower in regular smokers [19]. Melatonin may modulate the effects of nicotine, because melatonin treatment in humans reduces withdrawal-induced craving among those who have stopped smoking but continue to suffer the effects of withdrawal [20]. Our hypothesis was that evening type is associated with higher nicotine dependence according to different ND measurements and nicotine intake level. Our aim was to replicate and extend earlier published associations concerning diurnal type and smoking by applying multiple measures of ND and level of nicotine intake. Using data from the population based National FINRISK 2007 Study we examined whether

smoking habits, ND measured by the FTND, the Hooked on Nicotine Checklist (HONC) [21] and the Nicotine Dependence Syndrome Scale (NDSS) [22] as well as plasma cotinine levels differ by diurnal type assessed by six items.

Methods

Participants

In 2007 the cross sectional FINRISK data and its subsample DILGOM data were collected. The FINRISK data include a representative sample targeting 11,953 individuals (67% participation rate) (aged 25 to 74 years) from six different regions of Finland [23] with 7993 participants. Thus 33% (n=3960) of the sample did not return the questionnaire and/or take a part of clinical examination. The FINRISK data collection includes a questionnaire and a clinical health examination. From each region, i.e. (1) Helsinki and Vantaa (the metropolitan area), (2) Turku and Loimaa, (3) Northern Savo, (4) North Karelia, (5) Oulu, and (6) Lapland participants were invited to fill in the questionnaire (regions # 1-6) and asked to participate into a locally organized health examination (regions # 1-5) including a blood sample. Data collection was conducted from January to March 2007. Number of participants with smoking information was 7883 (3682 men, 47%) and diurnal type information was provided by 7091 persons, comprising the final number used in the analyses.

Participants of the DILGOM study, a FINRISK sub-sample were identified based on their responses to the FINRISK smoking questions. In three aforementioned regions (# 1-3) individuals who answered positively to the question “Have you ever smoked at least 100 cigarettes during your lifetime?” were selected, including daily, occasional and former smokers. In two regions (# 4-5) those who answered positively to the question “Are you a current smoker?” were selected, including daily and occasional smokers. These ever smokers (n=1922) received a questionnaire with detailed smoking and ND assessments while they visited the DILGOM survey site. This procedure took place from April to June 2007. Participants returned the completed questionnaires by mail and one round of reminder questionnaires was mailed to non-respondents in November 2007. Total of 1746 ever smokers participated (91%), comprising the final number used in the analyses.

The FINRISK 2007 study (20.2.2007/229/E0/06) has been approved by the Coordinating Ethics Committee (Institutional Review Board) of the Hospital District of Helsinki and Uusimaa.

Assessment

Diurnal type was assessed with six questions derived from the original, biologically verified Horne-Östberg Morningness-Eveningness Questionnaire (MEQ) of 19 items [24] and whose sum score correlates with the intrinsic circadian period, demonstrating that a basic property of the circadian pacemaker associates with this behavioral trait [25,26]. Questions included items on the most pleasant period of the day to work and to do hard physical task or sport exercise, the easiness to wake up in the morning, how tired one feels after awakening in the morning, and how to rate oneself as early bird (morning type) or night owl (evening type). Since the circadian preference in the present study was assessed with a modified questionnaire, the psychometric properties were tested. Six items of the original MEQ were selected on the basis of regression analysis of the items that correlated best with the sum [11], with which 83% of the variation in the sum was explained. Internal consistency of the six item scale (Cronbach α=0.78) was adequate. In this study the scored sum scale ranged from 5 (evening type) to 27 (morning type) and the mean was 17.8 (SD 4.2). The sum score (low score indicating eveningness) on the scale was divided into three categories, including the evening (category 3) (definite/moderate) (5-12 points), intermediate (category 2) (13-18

points), and morning (category 1, reference group) (definite/moderate) (19-27 points) chronotypes. This categorization converts the original five-point Morningness-Eveningness scale [24] into a three-point scale and retains the corresponding ranges for chronotypes.

Smoking status was assessed in FINRISK data by three questions: “Have you ever smoked regularly, almost every day for at least a year?”, “Do you smoke now?” and “When was the last time you smoked?” providing categories of daily smokers (smoked today or at least yesterday), occasional smokers (smoked two days to a month ago), former smokers (quit one month ago or earlier), and never smokers (never smoked regularly). In the analysis two classifications of smoking were used. First the category of “current smokers” included daily and occasional smokers whereas “non-smokers” included former and never smokers. Secondly “ever smokers” included current and former smokers, while “never smokers” were those who had never smoked regularly. Cigarettes per day variable included the sum of both manufactured and self-rolled cigarettes asked by two open-ended questions “How much on average per day do you smoke or did you smoke before you quit?”.

Measurements of ND included the six-item FTND scale [8] (ranging from 0 to 10), the 10-item HONC (from 0 to 10) [21], and the 14-item NDSS (from 0 to 56) [22]. Higher scores mean greater ND in all three scales. Each sum score was used as dependent continuous variable.

For 645 current smokers belonging to the DILGOM subsample cotinine from blood samples taken during the clinical examination was used as biochemical measurement of nicotine metabolites. Cotinine was analysed with a gas chromatograph-mass spectrometer (GC-MS). (-)-Cotinine was purchased from Sigma-Aldrich (Steinheim, Germany) and cotinine methyl-D3 (internal standard, IS) from Toronto Research Chemicals (Toronto, Canada).

The frozen plasma samples were thawed over night at +5°C. Cotinine was extracted from 0.5 ml aliquots of the samples with Oasis® MCX 3 cc (Waters; New Bedford, MA, USA) solid phase extraction cartridges as follows: the cartridges were first conditioned with 1 ml of methanol and 1 ml of purified water, and then samples were loaded on the cartridges with 2.5 ml of 0.3 M NaH_2PO_4 buffer containing the IS. Cartridges were washed with 1 ml of purified water and 1 ml of acetonitrile, dried for 1.5 min, and eluted with 3-% NH_3 into test tubes containing Na_2SO_4. The eluates were transferred to clean test tubes and evaporated to dryness with a vacuum evaporator. After dissolving the residues in 60 μl of butyl acetate, 15 μl of the derivatization reagent, N-methyl-N-trimethylsilyltrifluoroacetamide (MSTFA) was added. Then, a 2-μl aliquot of the sample was injected into a gas GC-MS.

The analysis was performed with a Hewlett-Packard (Hewlett-Packard Company, Palo Alto, CA, USA) GC-MS (EI, positive ions, 70 eV). The GC column was a DB-17 ms of length 20 m, internal diameter 0.18 mm and film thickness 0.18 μm (J&W Scientific Inc., Folsom, CA, USA). Helium was used as the carrier gas. The column temperature was initially 120°C with a hold time of 3 min, and was increased 45°C/min to 300°C. MS detection was performed in selected ion monitoring (SIM) mode.

The lower limit of quantitation was set at 5.0 μg/L. Intermediate precision (relative standard deviation, RSD %) was 3% and accuracy (bias %) was 4% at the concentration level of 100 μg/L. At the lower limit of quantitation the corresponding values were 7% and -2.3%, respectively.

Participants invited to the clinical examination were told to fast but were not asked to abstain from smoking before the examination [27]. The time since the last cigarette was asked from all by the study nurse: “Have you smoked in one hour before the clinical examination?”. Four percent (3.7%) of 645 current smokers reported that they had smoked

within one hour before clinical examination. Clinical examinations took place between 10:55 a.m. and 8:10 p.m., with the mean time of the clinical examination being 2:50 p.m. with no significant difference between chronotypes.

Potential confounders controlled in this study were alcohol use and depressive symptoms [10,13]. Alcohol use was assessed using the last week's recall on alcohol consumption and calculated as grams per week (continuous variable). Depressive symptoms were measured with having a positive response to the two screening items of depression: the presence of depressed mood and/or the presence of anhedonia and lack of pleasure at least for two weeks during past year (variable of three categories) [28,29].

Statistical analyses

Logistic regression analysis was used to examine the association between diurnal type categories (independent) and smoking status (dependent). Linear regression was used to examine the association between diurnal type continuous score (quantified as a z-score, i.e. mean of 0 and standard deviation of 1) and continuous ND measurements and cotinine values. To test the linearity of the association, higher order polynomials (quadratic and cubic) of diurnal score were also fit to the regression model. Multinomial logit modeling was used to examine the association between diurnal type category and categorical time to first cigarette (TTF, single item of FTND scale) variable. Interaction of diurnal type and sex was also tested (nested models likelihood), and where significant, sex-specific analyses are reported. All models were adjusted for age and sex. Further adjustment for alcohol use and depression were used to test whether the association between diurnal type and ND was independent of alcohol use and depression. The data analyses were performed with Stata (version 11) statistical software [30].

Results

FINRISK sample

The total number of participants with both diurnal type and smoking status information was 7091 (Table 1). About 12% of individuals in FINRISK data were evening types and 48% were morning types. The prevalence of current smokers (daily or occasional) was higher among evening types (37%) than in morning types (22%) (Table 2). Similarly the proportion of ever smokers (current or former) was larger in evening types (62%) than in morning types (54%). Similar patterns were found among both men and women.

In order to assess any non-response bias we analyzed if missing data on diurnal type depended on smoking status in FINRISK data. Information on diurnal type was missing in about 10% of current smokers, 9% former smokers and 10% never smokers. The distribution of smoking status did not differ between those with and without diurnal type (age-sex adjusted logistic regression p-value=0.38).

In this study sample about six per cent of men used 24 or more alcoholic drinks and two percent of women used 16 or more drinks per week. Twenty six per cent of men and 42% of women used no alcohol during previous week. The average use was 7.9 (10.4 SD) drinks per week in men and 3.2 (6.2 SD) drinks in women. About 14% of participants (11% of men and 16 % of women) had depressive symptoms by two screening questions.

Logistic regression analyses of smoking status and diurnal type

Risk for being a current smoker (*vs.* non-smoker) (n=7091) and ever smoker (*vs.* never smoker) (n=7091) for evening types compared to morning types was analyzed by logistic regression. These analyses were adjusted for age and sex and in addition in separate models

for alcohol use and depressive symptoms (Table 3). The odds ratio (OR) of being a current smoker among evening types was 1.66 (95% CI 1.40, 1.97) compared to morning types. No gender by diurnal interaction was found (p=0.79).

Results remained significant although the effect size decreased marginally when adjusted for alcohol use (OR=1.51, 95% CI 1.26, 1.80). The association weakened a bit more when adjusted for depression (OR=1.45, 95% CI 1.22, 1.73). Further attenuation was observed when adjusted simultaneously for both potential confounders (OR=1.35, 95% CI 1.12, 1.61), but the association remained significant (Table 3). Relatively small changes in risk estimates among current smokers indicated that alcohol use and depressive symptoms did not account for the association of diurnal type with current smoking.

The OR of being ever smoker among evening types was 1.42 (95% CI 1.20, 1.67) times higher compared to morning types (Table 3). There was a significant (p=0.01) gender by diurnal type interaction for ever-smoking and gender-specific analyses were performed. Among men age adjusted OR of being an ever smoker among evening types was 1.34 (95% CI 1.03, 1.74) and among women 1.51 (95% CI 1.22, 1.86). The OR became non-significant among men when adjusted for alcohol use and depression indicating that among men the association between diurnal type and ever smoking is not fully independent of those confounders.

DILGOM subsample of the FINRISK study

In the DILGOM subsample 13% were evening types and 47% morning types. We assessed the representativeness of the DILGOM subset by comparing the risk of being a current smoker by diurnal type in the total FINRISK sample and the DILGOM subset. As never smokers were not present (by design) in DILGOM data, we computed logistic regression analyses having current *vs.* former smoker as outcome variable in both data sets. The age and sex adjusted OR of being a current smoker among evening types compared to morning types in FINRISK data was 1.59 (95% CI 1.29, 2.00) and in DILGOM data 1.42 (95% CI 1.02, 1.20).

In DILGOM data three ND measurements, the FTND, the HONC, and the NDSS were used. In addition plasma cotinine levels, reflecting nicotine intake, were measured among current smokers. Descriptive statistics by diurnal type are given in Table 4 for current and former smokers. The correlation between FTND and HONC was 0.56, between FTND and NDSS 0.69, and between HONC and NDSS 0.57. Among current smokers the correlations between cotinine and FTND (r= 0.55), HONC (0.32) and NDSS (0.45) were more modest.

We used linear regression to examine the association between diurnal type score (continuous variable z-score) and ND measurements (in ever smokers) and cotinine (square root transformation to normalize the distribution) among current smoking participants (Table 5). Significant gender by diurnal interactions for FTND (p=0.04) and cotinine (p=0.008) were found but not for HONC (p=0.25) or NDSS (p=0.88). To test the linearity of the association, we added quadratic and cubic terms for diurnal type score, but these higher order models did not result in a significant improvement in model fit (likelihood ratio test), suggesting that simple linear models fitted best to the data.

Linear regression showed significant association for diurnal type and FTND only in men whereas for diurnal type and HONC significant association was seen for sexes combined. Associations remained significant even after adjustment for alcohol use and depression. When analyzing NDSS as dependent variable a significant association with diurnal type was seen that remained after adjustment for alcohol use but further adjustment for depression attenuated this association significantly (Table 5).

Using cut-point of 4 or more on the FTND 40% of current smokers were ND (mean 3.0, SD 2.6). Among current smokers 48% of evening types were nicotine dependent compared to 40% of intermediate types and 38% of morning types. The age and sex adjusted OR of being dependent on nicotine among evening types measured by FTND (≥4) was 1.82 (95% CI 1.18, 2.83). Adjusting for both alcohol use and depressive symptoms the risk among evening types was attenuated but remained significant 1.59 (95% CI 1.01, 2.51).

Cotinine levels were highest among evening type group of current smokers (Table 4), and a significant sex by diurnal type interaction was seen in the linear regression model. The association was significant only among men remaining significant after adjustment for alcohol use and depression (Table 5).

To help assess the relative impact of diurnal type on different measures of ND, effect sizes with standardized linear regression coeffcients were computed (ND was dependent while diurnal type was independent variable, adjusted for age and sex). Standardized estimates indicated rather similar effect sizes of all ND measurements and nicotine intake, the FTND (0.12), the HONC (0.11), the NDSS (0.14) and cotinine (0.10).

As one of the FTND scale's six items, the TTF is showed to be a predictor of smoking cessation [31], relapse [32] and is associated with higher cotinine levels [33] we examined item of this scale among morning and evening type groups. Sixteen per cent of evening types light up cigarette within 5 minutes after waking, compared to 8% of morning types. Based on multinominal regression the OR of lighting up first cigarette in the morning within first five minutes among evening types was three times (OR=2.95, 95% CI 1.74, 4.98) higher compared to morning types. The risk decreased slightly when alcohol use (OR=2.82, 95% CI 1.66, 4.78), depression (OR=2.33, 95% CI 1.35, 4.01) and both confounders together (OR=2.25, 95% CI 1.31, 3.89) were included into the analyses, but remained elevated and highly significant. This indicates that alcohol use and depression did not account for the association between diurnal type and TTF.

Discussion

Evening type is associated with daily smoking and ever smoking, higher scores on ND measured by FTND, HONC and NDSS and plasma cotinine levels compared to morning types. Association between evening type and smoking has been reported earlier [3,4,6,34] as well as association between evening type and ND measured by number of DSM-IV symptoms and FTND [7].

Associations of evening type with current and ever smoking remained after adjustment for two potential confounders, alcohol use and presence of depressive symptoms during past year. Adjustment for alcohol use and depression did not change results except that depression attenuated the association of diurnal type with NDSS.

About 12% of individuals were evening types and 48% were morning types. An earlier study found that 10% of participants to be clearly evening persons and 30% to be clearly morning persons [7]. In the present study, diurnal type was measured with a six-item sum scale derived from the Horne-Ostberg Morningness-eveningness questionnaire [24]. Earlier Finnish studies [2,6,7] have measured this behavioral trait with a single question with four alternative responses derived from the Torsvall-Akerstedt Diurnal type scale [35], yielding no information about the intermediate types. Nonetheless the current study and the study on Finnish adult twins show similar proportions of evening types.

Diurnal type is biologically determined but environmentally modified, about half of its variation being explained by genetic effects [2,36]. This behavioural trait reflects the

function of the circadian pacemaker that generates both the circadian rhythms and the seasonal variations in mood and behavior [37] and interacts with the homeostatic sleep process to produce the sleep-wake cycle. Concerning smoking behavior, nicotine is a direct agonist of nAChRs and activates mesolimbic dopaminergic pathways [17]. In this reward circuit, activation of the enzyme monoamine oxidase A is regulated by the circadian pacemaker and Period 2 gene (PER2) abundance stimulates the transcription, leading to reduced levels of dopamine and a predisposition to depressive-like behaviours [38,39], and this compromises the feedback [40-42]. It is of note that there is a link between the PER2 gene variants and higher levels of alcohol use through the glutaminergic system [13], and glutaminergic receptor genes associate with smoking behaviour as well [43,44]. Nicotine is also a psychoactive stimulant, and this could make smokers more alert, delay the phase of circadian rhythms and keep them staying up later. Clearly, there is a need for mechanistic studies that analyze a biologically-based measure of diurnal type in relation to genetic data.

Diurnal type has been associated with anxiety [45], attention-deficit/hyperactivity disorder (ADHD) [46] and depression [10,47-50], while depression is associated with a higher prevalence of smoking [51,52]. In our earlier paper [7] mood and depression were assessed with life satisfaction and the number of DSM-IV depression symptoms, and we found no evidence that depression would confound the association between diurnal type and ND. In the present study the adjustment for depression, based on two screening questions [29], attenuated the strength and significance of the association. Mostly the association remained highly significant, but the adjustment attenuated the association of diurnal type with NDSS. This suggests that depression may confound the relationship between diurnal type and ND measured with the NDSS. There may be a component of ND correlated with depression and diurnal type captured by NDSS but not by other ND measures. This highlights the importance of using multiple measures of ND as there is no single golden standard measure. However, whether depression, instead of confounding, might actually mediate the association between diurnal type and ND, remains a challenge of further research, because mediation can be tested reliably only in a longitudinal design [53]. It is possible that socioeconomic status (SES) could be associated to diurnal type. However, in present study adjustment for SES did not diminish the strength and association as reported earlier [54].

ND measurements included the widely used FTND scale [8] which assesses physical dependence and predicts relapses [55]. ND was also measured by the HONC identifying a loss of autonomy in smoking [21]. In addition, the multidimensional NDSS was used assessing drive, priority, continuity, stereotype and tolerance [22]. As linear regression analysis with adjustment of depressive symptoms attenuated the association of diurnal type with NDSS and not with FTND or HONC it seems that this multidimensional association between ND and depression needs further examination. In the earlier study we used also FTND and no attenuation was seen between diurnal type and FTND scale when adjusted for number of DSM-IV symptoms of depression. FTND and HONC scales are unidimensional whereas NDSS is multidimensional with physiological, psychological and social dependency items, having five or less subscales depending on data [22].

The associations of FTND and cotinine levels with diurnal type showed similar patterns. Both showed significant sex interactions, with stronger associations in men than in women. A central element of FTND is amount smoked daily, which is also indexed by cotinine levels [56]. The other central element of FTND is TTF, which together with amount smoked accounts for some 80% of the variance in FTND, and the two together forms the Heaviness of Smoking Index scale [57]. Moreover, we found that risk for evening types to light up the first cigarette in the morning within five first minutes after waking was three times higher compared to morning types. This could possibly be due to higher ND overall or worse capability to tolerate decreased morning level of nicotine in circulation causing more severe

physical withdrawal symptoms. Interestingly, a study of adult smokers in the UK indicated that the first cigarette of the day and smoked cigarettes during the night are inhaled less intensively [58]. Our earlier study shows [7] that heavy smoking (>20 cigarettes per day) is associated with evening type. The present study is in line with that finding. The current finding indicates that higher cotinine levels and higher FTND score (including cigarettes per day item) are related to evening type. It is noteworthy that associations of evening type with cotinine and FTND were significant only among men, possibly due to the fact that daily cigarette consumption of men is higher.

FINRISK and DILGOM data have several strengths. FINRISK is a representative large population-based sample collected in 2007 and thus represents well the existing smoking prevalence in Finland. Also the DILGOM subsample appears to represent the population well as the association of diurnal type and smoking status was similar to that in the whole dataset. An additional strength is that study applied multiple ND measures and cotinine levels derived from population data.

The possible causality behind the observed association remains unknown as a cross-sectional survey does not provide adequate design to determine causality for the association between diurnal type and smoking. Follow-up data is needed in order to address this question. Longitudinal studies are required to assess the changes and interdependencies in diurnal type, smoking habits and ND. Also other types of studies are needed for example observing the behavior, peer interaction and other substance use, alcohol and drugs, of evening and morning types in adolescence, when smoking commonly is initiated. In addition, as in our study the information on diurnal type is derived from a self-report, there is a further need for studies that use a biologically-based measure of diurnal type or that of rest-activity cycle for assessment.

The results observed in the older Finnish Twin Cohort data were replicated and extended. This study further supports earlier finding, that evening type is an important determinant of ND and associated with multiple ND measures and nicotine intake. Evening type persons are at higher risk of dependence, although depressive symptoms to some extent attenuate this risk. Understanding the factors underlying the associations between chronotype and ND could provide novel insights into the mechanisms of nicotine addiction.

Acknowledgments

This work was supported by the Juho Vainio Foundation and the Yrjö Jahnsson Foundation to U. Broms and a National Institutes of Health (NIH) grant (grant number DA12854) to P.A.F. Madden and J. Kaprio.

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Abbreviations

FTND	Fagerström Test for Nicotine Dependence
NDSS	Nicotine Dependence Syndrome Scale
HONC	Hooked on Nicotine Checklist
DILGOM	The Dietary, Lifestyle and Genetic Determinants of Obesity and Metabolic Syndrome Substudy
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th edition
EI	Electron Ionization
GC-MS	Gas Chromatograph – Mass Spectrometer
IS	Internal Standard
nAChR	Nicotinic Acetylcholine Receptor
ND	Nicotine Dependence
RSD	Relative Standard Deviation

SES	Socioeconomic Status
SIM	Selected Ion Monitoring
TTF	Time to First Cigarette in the Morning (One Item of FTND Score)

Table 1

Number of individuals (%) in each smoking status group by diurnal type in FINRISK data (n=7091).

Smoking status		Morning type	(%)	Intermediate type	(%)	Evening type	(%)	All	(%)
Current	Daily	748	(22.1)	696	(24.1)	204	(36.9)	1748	(24.6)
	Occasional	541	(16.0)	479	(16.6)	221	(26.8)	1 241	(17.5)
		207	(6.1)	217	(7.5)	83	(10.1)	507	(7.1)
Former		1071	(31.6)	806	(28.0)	208	(25.2)	2085	(29.4)
Never		1569	(46.3)	1377	(47.8)	312	(37.9)	3258	(45.9)
Total		3388		2879		824		7091	

Table 2

Proportion (%) of current (=daily and occasional) and ever (=current and former) smokers by diurnal type in FINRISK data (n=7091) among all participants and by sex.

	All	Men	Women
Current smokers			
Morning type	22.1	26.3	17.9
Intermediate type	24.1	29.5	20.1
Evening type	36.9	44.9	31.3
	n=7091	*n*=3264	*n*=3827
Ever smokers			
Morning type	53.7	65.7	42.0
Intermediate type	52.1	62.0	44.7
Evening type	62.1	70.1	56.5
	n=7091	*n*=3264	*n*=3827

Table 3

Logistic regression odds ratios (and 95 % confidence intervals) for risk of being current smoker (*vs.* non-smoker) and ever smoker (*vs.* never smoker) in FINRISK data among evening types compared to morning types. Each row shows the variables included in the model. Age is included in all models and sex only when men and women were analyzed together.

Evening type *vs.* Morning type	**OR for Current smoking *vs.* Non-smoking**			**OR for Ever smoking *vs.* Never smoking**		
Models adjusted for:	**All**	**Men**	**Women**	**All**	**Men**	**Women**
Age and sex	1.66 (1.40, 1.97)	1.68 (1.31, 2.16)	1.65 (1.30, 2.09)	1.42 (1.20, 1.67)	1.34 (1.03, 1.74)	1.51 (1.22, 1.86)
Alcohol use[a]	1.51 (1.26 1.80)	1.54 (1.19,1.99)	1.42 (1.11, 1.82)	1.31 (1.11, 1.55)	1.25 (0.96, 1.63)	1.35 (1.10, 1.67)
Depression[b]	1.45 (1.22, 1.73)	1.47 (1.33, 1.90)	1.44 (1.13, 1.83)	1.28 (1.08, 1.51)	1.18 (0.91, 1.54)	1.38 (1.12, 1.71)
Alcohol use and depression	1.35 (1.12, 1.61)	1.38 (1.06, 1.80)	1.27 (1.00, 1.63)	1.20 (1.02, 1.42)	1.12 (0.86, 1.47)	1.26 (1.01, 1.56)

[a] Grams / week (continuous variable)

[b] Two screening questions: Positive response to two brief items of depression (presence for two weeks during past year depressed mood and / or anhedonia) (variable of three categories)

J Addict Res Ther. Author manuscript; available in PMC 2012 August 17.

Table 4

Means (and standard deviations) of the FTND, the HONC, the NDSS and plasma cotinine levels (μg/L) (cotinine information available only on current smokers) in three diurnal type groups among current smokers (n=712) and former smokers (n=633) in DILGOM sub-sample of the FINRISK study.

		FTND Mean (SD)	HONC Mean (SD)	NDSS Mean (SD)	Cotinine (μg/L) Mean (SD)
Current smokers	Morning type	3.04 (2.42)	5.24 (2.92)	17.2 (7.44)	146 (97.3)
	Intermediate type	2.84 (2.55)	5.41 (2.89)	16.6 (8.44)	144 (97.9)
	Evening type	3.54 (3.00)	5.98 (3.08)	19.3 (10.43)	161 (107)
Former smokers	Morning type	2.13 (2.26)	3.49 (2.87)	16.8 (7.69)	n.a.*
	Intermediate type	2.04 (2.20)	3.69 (2.93)	16.8 (8.02)	n.a.
	Evening type	2.64 (2.76)	4.48 (3.29)	19.1 (9.80)	n.a.

*Cotinine information available only on current smokers

FTND=the Fagerström Test for Nicotine Dependence, HONC=the Hooked on Nicotine Checklist, NDSS=the Nicotine Dependence Syndrome Scale

Table 5

Linear regression analysis (beta-coefficient and 95% confidence intervals) of the Fagerstrom Test for Nicotine Dependence (FTND, n=712), the Hooked on Nicotine Checklist (HONC, n=781), the Nicotine Dependence Syndrome Scale (NDSS, n=781) and cotinine (n=645) with respect to diurnal score (continuous variable z-score) among current smoking participants in DILGOM data.

Diurnal type adjusted	**FTND**		**HONC***	**NDSS***	**Cotinine**	
	Men	**Women**			**Men**	**Women**
Age (sex*) -	-0.46 (-0.72, -0.21)	-0.02 (-0.27, 0.25)	-0.31 (-0.52, -0.11)	-0.86 (-1.43, -0.29)	-0.73 (-1.16, -0.29)	0.11 (-0.36, 0.59)
Age (sex), Alcohol use[a]	-0.46 (-0.72, -0.20)	-0.002 (-0.26, 0.26)	-0.30 (-0.50, -0.10)	-0.79 (-1.37, -0.21)	-0.75 (-1.19, -0.32)	0.11 (-0.37, 0.59)
Age (sex), Depression[b]	-0.37 (-0.62, -0.11)	0.06 (-0.19, 0.31)	-0.21 (-0.42, -0.01)	-0.55 (-1.12, 0.02) -	-0.67 (-1.11, -0.22)	0.09 (-0.38, 0.57)
Age (sex), Alcohol use, depression	-0.37 (-0.63, -0.12)	0.06 (-0.19, 0.32)	-0.21 (-0.41, 0.002)	-0.50 (-1.07, 0.08)	-0.69 (-1.14, -0.24)	0.09 (-0.39, 0.57)

*Sex was adjusted when the HONC and the NDSS scales were analyzed due to no significant interactions by sex.

[a]Grams / week (continuous variable)

[b]Two screening questions: Positive response to two brief items of depression (presence for two weeks during past year depressed mood and / or anhedonia) (variable of three categories)

J Addict Res Ther. Author manuscript; available in PMC 2012 August 17.